

REMARKS

1. Applicants hereby submit the following:
- [] a paper copy of a "Sequence Listing", complying with §1.821(c), to be incorporated into the specification as directed above;
 - [XX] an amendment to the paper copy of the "Sequence Listing" submitted on November 13, 2001, the amendment being in the form of substitute sheets;
 - [XX] the Sequence Listing in computer readable form, complying with §1.821(e) and §1.824, including, if an amendment to the paper copy is submitted, all previously submitted data with the amendment incorporated therein;
 - [] pursuant to §1.821(e), reference is made to the computer readable form filed on , in USSN , which presents the identical Sequence information, the use of which is now requested, in lieu of submitting a new computer readable form; and/or
 - [] a substitute computer readable form to replace one found to be damaged or unreadable.

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[XX] 2. The description has been amended to comply with §1.821(d).

3. The undersigned attorney or agent hereby states as follows:

- (a) this submission is not believed to include new matter [§1.821(g)];
- (b) the contents of the paper copy (as amended, if applicable) and the computer readable form of the Sequence Listing, are believed to be the same [§1.821(f) and §1.825(b)];
- (c) if the paper copy has been amended, the amendment is believed to be supported by the specification and is not believed to include new matter [§1.825(a)]; and
- (d) if the computer readable form submitted herewith is a substitute for a form found upon receipt by the PTO to be damaged or unreadable, that the substitute data is believed to be identical to that originally filed [§1.825(d)].

4. Under U.S. rules, each sequence must be classified in <213> as an "Artificial Sequence", a sequence of

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"Unknown" origin, or a sequence originating in a particular organism, identified by its scientific name.

Neither the rules nor the MPEP clarify the nature of the relationship which must exist between a listed sequence and an organism for that organism to be identified as the origin of the sequence under <213>.

Hence, counsel may choose to identify a listed sequence as associated with a particular organism even though that sequence does not occur in nature by itself in that organism (it may be, e.g., an epitopic fragment of a naturally occurring protein, or a cDNA of a naturally occurring mRNA, or even a substitution mutant of a naturally occurring sequence). Hence, the identification of an organism in <213> should not be construed as an admission that the sequence *per se* occurs in nature in said organism.

Similarly, designation of a sequence as "artificial" should not be construed as a representation that the sequence has no association with any organism. For example, a primer or probe may be designated as "artificial" even though it is necessarily complementary to some target sequence, which may occur in nature. Or an "artificial" sequence may be a substitution mutant of a natural sequence, or a chimera of two or more natural sequences, or a cDNA (i.e., intron-free

sequence) corresponding to an intron-containing gene, or otherwise a fragment of a natural sequence.

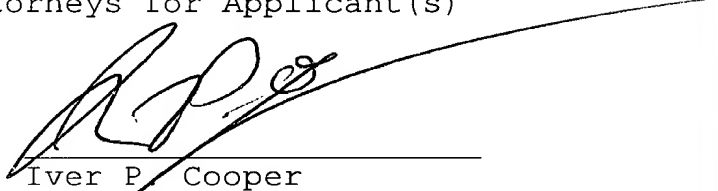
The Examiner should be able to judge the relationship of the enumerated sequences to natural sequences by giving full consideration to the specification, the art cited therein, any further art cited in an IDS, and the results of his or her sequence search against a database containing known natural sequences.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "Version with markings to show changes made".

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the specification:

The paragraph beginning at line 3 of page 10 has been amended as follows:

Fig 1. Alignment of 30 ACBP sequences (numbered consecutively from top to bottom as SEQ ID NOs:-1---30). The alignments are ~~done~~ with respect to the bovine sequence (SEQ ID NO:1) with residues Ser 1 to Ile 86. The lengths of the other sequences are indicated as a subscript after the last residue shown and the four helices of bovine ACBP are shown as boxes above the sequences. Conserved Class 1 residues are present in 18 out of the 21 l- and b-ACBPs and are highlighted by black boxes. Conserved class 2 residues are hydrophobic residues (either M/L/H/P/A/F/Y/V/I) in all l- and b-ACBP sequences and in at least 27 out of all 30 sequences and are highlighted by grey boxes. Cysteines are in white text in grey boxes. Yeast(1) is from *Saccharomyces cerevisiae* and Yeast(2) from *Saccharomyces monoasensis* and from *Saccharomyces pastoranis* (identical).

Table 1 beginning at line 18 of page 48 has been amended as follows:

Table 1 Primers used for site directed mutagenesis of bovine ACBP

Mutation	Sequence
<u>M24C</u>	
Upstream	5'-TGCTTGTTTCATCTACTCTCACTACAAG (SEQ ID NO:31)
Downstream	5'-TTCTTCGTCGGCCGGCTTGGTCTTC (SEQ ID NO:32)
<u>M46C</u>	
Upstream	5'-TGCTTGGACTTCAAGGGTAAGGCTAAG (SEQ ID NO:33)
Downstream	5'-CCCGGGTCTTTCGGTGTTGATGTC (SEQ ID NO:34)
<u>A53C</u>	
Upstream	5'-TGCAAGTGGGACGCTTGGAACGAATTG (SEQ ID NO:35)
Downstream	5'-CTTACCCTTGAAGTCCAACATCCC (SEQ ID NO:36)

The paragraph beginning at line 13 of page 57 has been amended as follows:

Recombinant *E. coli* fatty acyl-CoA ~~synthetase~~ synthetase was expressed as a N-terminal GST-fusion protein. The open reading frame of the *E. coli* fatty acyl-CoA ~~synthetase~~ synthetase was amplified using the pN3576 plasmid as template (Black et al., 1997) and specific oligonucleotides 5'-CACGGATCCATGAAGAAGGTTTGGCTTAACC-3' (SEQ ID NO:37) and 5'-CACGAATTCTCAGGCTTTATTGTCCACTTTG-3' (SEQ ID NO:38), carrying

either a *Bam*H1 and *Eco*R1 restriction site (underlined), respectively. The Expand High Fidelity PCR System was used as described by the manufacturer (Roche). The PCR product was digested with *Eco*R1 and *Bam*H1 and ligated into the pGEX-2TK vector (Pharmacia) using standard techniques. The recombinant GST-fusion protein was expressed in *E. coli* BL21(DE3) strain and purified essentially as described by the manufacturer (Pharmacia), except that CoA (10 mM) was included in all buffers including the elution buffer.

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